

Bayer 10,159,3-HCL
Le A 33 364 US-01 Lin/SWo

AMENDMENTS TO THE SPECIFICATION

Please add the Abstract attached to the end of this communication after page 127 of the application (i.e. after the claims of the originally filed application).

Please substitute pages 98-105 with amended pages 98-105 (see next page):

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WO 00/41469

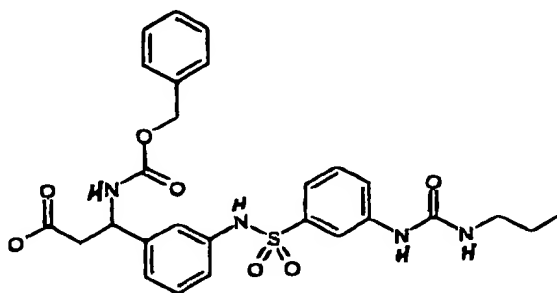
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acetonitrile, 13 min = 80 % acetonitrile, 15 min = 80% acetonitrile, 17 min = 10% acetonitrile.

Example 48

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(3R,S)-3-Benzoyloxycarbonylamino-3-{3-[3-(3-propyl-ureido)-phenylsulfonylamino]-phenyl}-propionic acid



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1.2 g of Wang polystyrene resin (Rapp-Polymere, Tübingen, loading 1.08 mmol/g) are swollen in dimethylformamide (DMF). The solvent is filtered off with suction and a solution of 841 mg (3R,S)-3-(9-Fluorenylmethoxycarbonylamino)-3-(3-nitrophenyl)-propionsäure in 15 ml dimethylformamide (DMF) is added. After shaking at room temperature for 15 min the suspension is treated with 350 µl of pyridine and 540 mg 2,6-dichlorobenzoylchloride. It is shaken over night at room temperature. The resin is then washed with dimethylformamide (DMF), methanol, dichloromethane.

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The resin is treated with 15 ml of a 20% strength piperidine solution in dimethylformamide (DMF). It is then washed 3 times with dimethylformamide (DMF) and a further 15 ml of a 20% strength piperidine solution in dimethylformamide (DMF). After shaking for 20 min., it is washed with dimethylformamide (DMF) and tetrahydrofuran (THF). The resin is treated with a solution of 450 µl diisopropylethylamine in 500 µl tetrahydrofuran (THF) and a solution of 330 mg benzylchloroformate (acylating / sulfonylating reagent) in 500 µl tetrahydrofuran (THF). It

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is shaken over night at room temperature. The resin is then washed with dimethylformamide (DMF), methanol, tetrahydrofuran (THF).

5 The resin is treated with a solution of 5400 mg tin(II) chloride dihydrate in 12 ml N-methylpyrrolidone (NMP) and shaken over night at room temperature. The resin is then washed with dimethylformamide (DMF), methanol, tetrahydrofuran (THF), dichloromethane.

10 The resin is treated with a solution of 450 µl diisopropylethylamine in 500 µl tetrahydrofuran (THF) and a solution of 430 mg 3-nitrobenzenesulfonylchloride in 500 µl tetrahydrofuran (THF). It is shaken over night at room temperature. The resin is then washed with dimethylformamide (DMF), methanol, tetrahydrofuran (THF).

15 The resin is treated with a solution of 5400 mg tin(II) chloride dihydrate in 12 ml N-methylpyrrolidone (NMP) and shaken over night at room temperature. The resin is then washed with dimethylformamide (DMF), methanol, tetrahydrofuran (THF), dichloromethane.

20 The resin is treated with a solution of 500 µl diisopropylethylamine in 12 ml tetrahydrofuran/dichloromethane 1:1 and a solution of 2757 mg 4-nitrophenylchloroformate in 12 ml tetrahydrofuran/dichloromethane 1:1. After 45 min. shaking at room temperature the resin is washed with tetrahydrofuran (THF) and dimethylformamide (DMF) and a solution of 943 mg propylamine (amine reagent) and 2780 µl diisopropylethylamine in 20 ml N-methylpyrrolidone (NMP) is added.
25 After shaking for 10 h the resin is washed with dimethylformamide (DMF), methanol, tetrahydrofuran (THF), dichloromethane.

30 For removal of the product, the resin is shaken with tetrahydrofuran/dichloromethane 1:1 for 1h, filtered off, and the filtrate is concentrated in vacuo and purified on silica gel. 148 mg of the title compound is obtained.

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Mass spectrometry (ESI): 555.

Retention time (HPLC): $R_t = 8,1$.

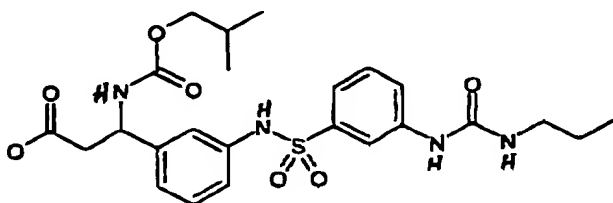
$^1\text{H-NMR}$ (400 MHz, methanol) $\delta = 7,90$ (s, 1H), 7,43 (d, 1H), 7,33 - 7,25 (m, 7H), 7,18 (s, 1H), 7,15 (d, 1H), 7,04 (d, 1H), 6,97 (d, 1H), 5,04 (dd, 1H, H-3), 5,03 (s, 2H), 3,12 (t, 2H), 2,72 (dd, 1H, H-2a), 2,65 (dd, 1H, H-2b), 1,52 (tq, 2H), 0,93 (t, 3H).

The following compounds can be prepared in analogy to example 48.

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Example 49

(3R,S)-3-iso-Butyloxycarbonylamino-3-{3-[3-(3-propyl-ureido)-phenylsulfonyl-amino]-phenyl}-propionic acid



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Mass spectrometry (ESI): 521.

Retention time (HPLC): $R_t = 8,4$.

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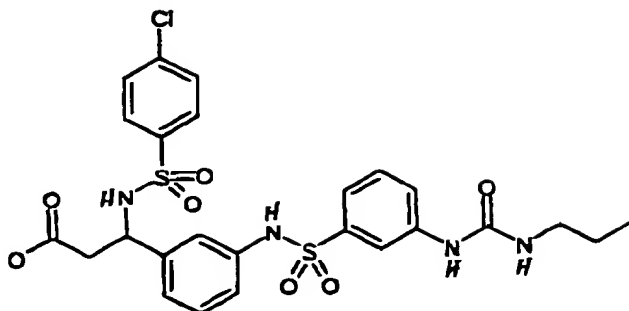
Example 50

(3R,S)-3-(4-Chlor-benzenesulfonylamino)-3-{3-[3-(3-propyl-ureido)-phenylsulfonyl-amino]-phenyl}-propionic acid

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Mass spectrometry (ESI): 596.

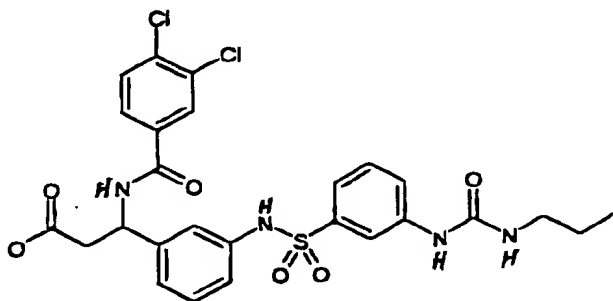
Retention time (HPLC): $R_t = 8.6$.

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Example 51

(3R,S)-3-(3,4-Dichlor-benzenecarbonylamino)-3-{3-[3-(3-propyl-ureido)-phenyl-sulfonylamino]-phenyl}-propionic acid

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Mass spectrometry (ESI): 594.

Retention time (HPLC): $R_t = 9.3$.

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Example 52

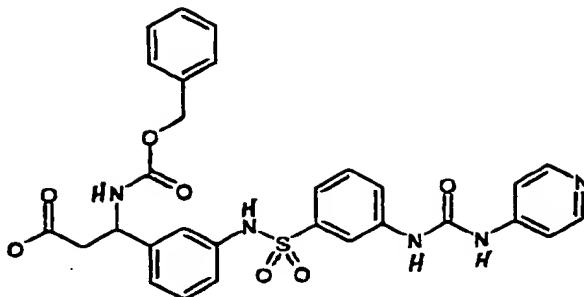
(3R,S)-3-Benzoyloxycarbonylamino-3-{3-[3-(3-pyridin-4-yl-ureido)-phenylsulfonylamino]-phenyl}-propionic acid

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Mass spectrometry (ESI): 590.

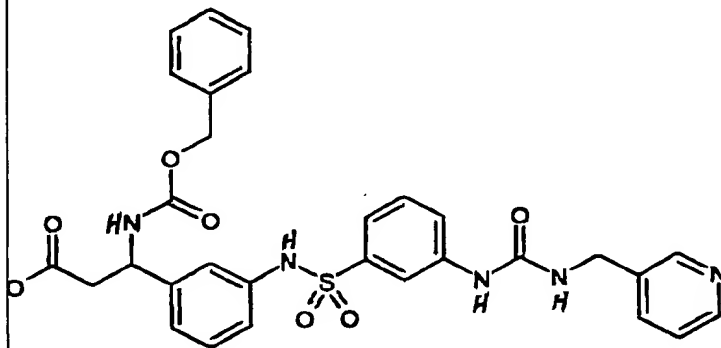
Retention time (HPLC): $R_t = 7.1$.

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Example 53

(3R,S)-3-Benzoyloxycarbonylamino-3-{3-[3-(3-pyridin-3-ylmethyl-ureido)-phenyl-sulfonylamino]-phenyl}-propionic acid

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Mass spectrometry (ESI): 604.

Retention time (HPLC): $R_t = 6.7$.

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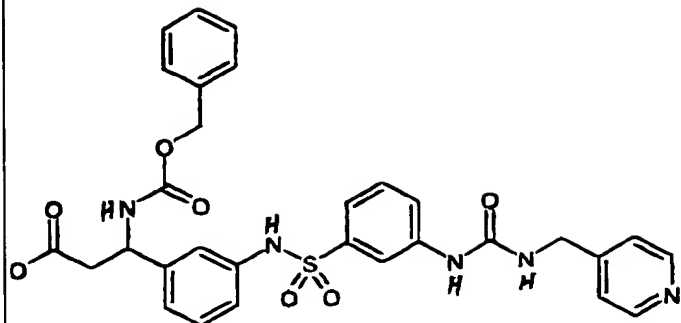
Example 54

(3R,S)-3-Benzoyloxycarbonylamino-3-{3-[3-(3-pyridin-4-ylmethyl-ureido)-phenyl-sulfonylamino]-phenyl}-propionic acid

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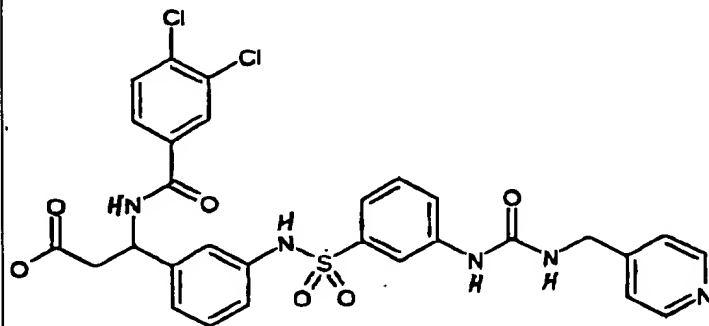
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Mass spectrometry (ESI): 604.

Retention time (HPLC): $R_t = 6,7$.**Example 55**

(3R,S)-3-(3,4-Dichlor-benzenecarbonylamino)-3-{3-[3-(3-pyridin-4-ylmethyl-ureido)-phenylsulfonylamino]-phenyl}-propionic acid



Mass spectrometry (ESI): 643.

Retention time (HPLC): $R_t = 7,2$.

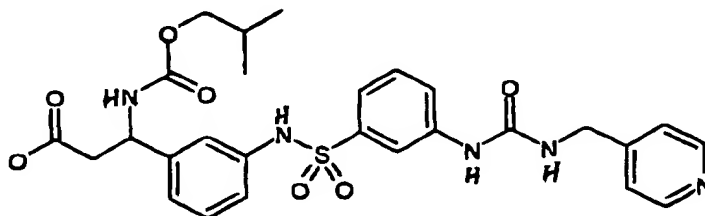
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Example 56

(3R,S)-3-(3,4-iso-Butyloxycarbonylamino)-3-{3-[3-(3-pyridin-4-ylmethyl-ureido)-phenylsulfonylamino]-phenyl}-propionic acid

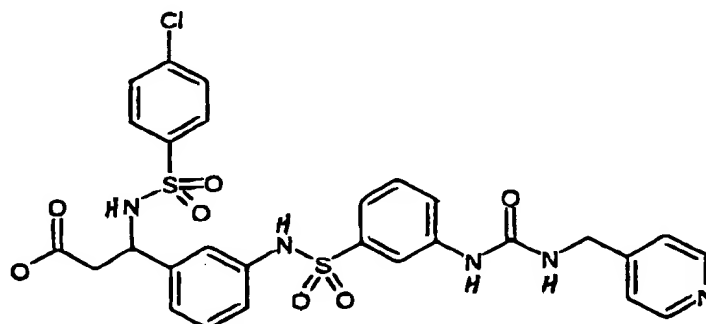


Mass spectrometry (ESI): 570.

Retention time (HPLC): $R_t = 7.2$.

Example 57

(3R,S)-3-(4-Chlor-benzenesulfonylamino)-3-{3-[3-(3-pyridin-4-ylmethyl-ureido)-phenylsulfonylamino]-phenyl}-propionic acid



Mass spectrometry (ESI): 644.

Retention time (HPLC): $R_t = 6.6$.

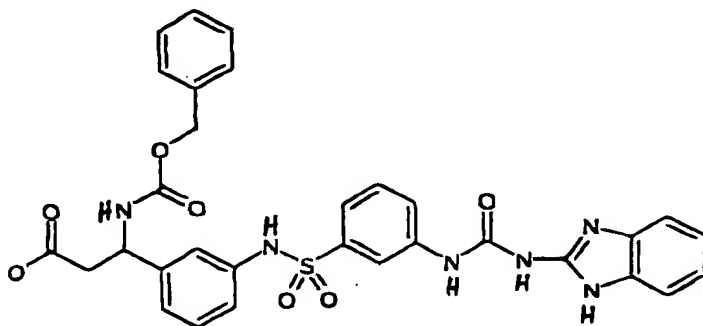
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Example 58

(3R,S)-3-Benzoyloxycarbonylamino-3-(3-{3-[3-(1H-Benzoimidazol-2-yl)-ureido]-phenylsulfonylamino}-phenyl)-propionic acid



Mass spectrometry (ESI): 629.

Retention time (HPLC): $R_t = 10,8$.